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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,482	11/19/2003	Naveen Arora	2761-0169P	3751

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/715,482	ARORA ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *9-19 and 22-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group I claims 1-8 and 21 with traverse is acknowledged. Claims 9-19 and 22-25 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claim 20 is cancelled.

Claim Objections

2. Claims 1-8 and 21 are objected to for the following informalities: "B. anthracis should be changed to "*Bacillus anthracis*" in the first occurrence in the claims and underlined or italicized. Correction is required.

3. Claim 21 is objected to for the following informalities: "Imperata cylindricum" should be changed to "*Imperata cylindrica*" and underlined or italicized. Correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1 and 3-8 are rejected under 35 U.S.C. 101 because they are directed to non-statutory subject matter. The claims are directed to a novel protein capable of inhibiting anthrax toxin activity. Claim 1 reads on a product that exists in nature. This rejection may be obviated, if the claims are amended to an "isolated or purified" novel protein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-8 and 21 are rejected under 35 U.S.C. 112, first paragraph as containing subject matter which lacks written description in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected to make and/or use the invention.

The claims are directed to a novel protein capable of inhibiting anthrax toxin activity. Dependent claims 2 and 21 recite "... wherein the protein is isolated from pollen grains of a grass of a genus selected from the group

consisting of *Imperata,* a genus related to *Imperata*, *Lolium*, a genus related to *Lolcium*, *Phleum*, a genus related to *Phleum*, *Cynodon* and a genus related to *Cynodon*" and "...wherein the grass is selected from the group consisting of *Imperata cylindrica, Lolium perenne, Phleum pretense* and *Cynodon datylon*". Therefore, the claims encompass a genus of 67 kDa proteins:

The specification only provides written description for the 67 kDa protein isolated from *Imperata cylindrica.* There is no disclosure that the claimed protein was isolated from a grass other than *Imperata cylindrica.* The instant specification does not describe a 67 kDa protein isolated from pollen grains of a grass of a genus selected from the group consisting of *Imperata,* a genus related to *Imperata*, *Lolium*, a genus related to *Lolcium*, *Phleum*, a genus related to *Phleum*, *Cynodon* and a genus related to *Cynodon*". The specification also fails to provide adequate written description for claimed protein isolated from *Lolium perenne, Phleum pretense* or *Cynodon datylon.*

Bijl et al (*Clin. Exp. Allergy, January 2003, 33:65-71)* teach a 67kDa protein purified from *Imperata cylindrica* (page 65). Verma et al *(International Archives of Allergy and Immunology, 2000, 122:251-256)* teach a 67kDa protein purified from *Imperata cylindrica* that binds IgE (page 252). Therefore, one of skill in the art would not conclude that the claimed novel 67-kda protein could be isolated from a grass other than *Imperata cylindrica.* One skilled in the art would not conclude that Applicant was not in possession of the claimed genus of 67 kDa proteins at the time of filing. Therefore, Applicant has not met the written description requirements as set forth in 35 U.S.C. 112, first paragraph.

6. Claims 1-8 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a novel protein capable of inhibiting anthrax toxin activity.

The specification teaches that the protein of the invention can inhibit activity of anthrax toxin (page 2). The specification teaches that the protein has the utility for developing a therapeutic agent that can reduce the toxic effects once the disease has set in (page 2). Therefore the instant specification contemplates the use of the claimed 67 kDa protein to treat anthrax *in vivo*. The specification only discloses inhibition studies *in vitro* using claimed 67 kDa protein incubated with J774A.1 (eukaryotic) cells (pages 7-8). The specification has failed to correlate *in vivo* treatment of anthrax using the claimed protein and the *in vitro* treatment of anthrax using the claimed protein. The specification teaches that the novel protein for inhibition of activity of anthrax and the purified protein has the ability or reduce the toxic effects of anthrax (page 2). What toxic effects are reduce? The toxic effects of PA or LF or both or other toxins? What constitutes a reduction? The specification and claims teach that the claimed 67-kDa protein has IgE binding properties. The specification further teaches that in *in vitro* assays using the claimed protein and *Imperata cylindrica* (Ic) hypersensitive individual's sera, 10 out of 12 sera demonstrated it to be a major

allergen (page 6 and Figure 2). Example 7 of the instant specification teaches that the 67 kDa protein was "preincubated" with the J774A.1 cell line in an *in vitro* assay. Therefore, a "preincubation" of the protein with the cells is required. How does this correlate with administering the 67 kDa protein *in vivo*? Will the protein effective *in vivo* if preincubation is not possible? How is the preincubation requirement met *in vivo*? Does the 67 kDa protein reach the reach the target site to inhibit the PA and LF antigens? Verma et al *(International Archives of Allergy and Immunology, 2000, 122:251-256)* teach that grass pollen allergens have been implicated in the induction of type I allergic disorders in atopic individuals (page 251). Verma et al teach that the 67 kDa protein isolated from *Imperata cylindrica* Pollen Extract showed high IgE binding in ELISA and reacted with 80% of the patients' sera and suggest that the 67 kDa protein may be a new allergen (page 255). Vieths et al (*Ann N.Y. Acad. Sci., 964:47-68, 2002)* teach that pollen-allergic patients frequently present allergic symptoms after ingestion of several kinds of plant-derived food (see the Abstract). Vieths et al teach that approximately 15-20% of the population in developed countries are allergic to pollen and 50-93% of birch pollen-allergic patients have IgE mediated reactions to pollen related foods (page 48). Vieths et al teach that at the molecular level, observations are based on the cross-reactions of human IgE antibodies which are directed against pollen allergens with homologous allergens in plant food (page 48). How would the claimed 67 kDa protein react when administered *in vivo* to patients that produce high levels of IgE neutralizing antibodies due to allergic reactions? Zhao et al *(Human Antibodies, 2003; 12(4):129-35)* teach that

neutralizing monoclonal antibodies can block the action of anthrax toxin lethal toxin factor formation (see the Abstract). If neutralizing antibodies are to LF are present, how does the effected the claimed protein when administered *in vivo*?

One of skill in the art could not have reason to doubt the assertion that the claimed 67 kDa protein would be effective in inhibiting anthrax in vivo based on the teachings of the cited art and the absence of evidence in the instant disclosure to correlate inhibition of the anthrax toxins with in vivo administration of the claimed protein.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to using the claimed protein to inhibit the anthrax toxin *in vivo* 3) there are no working examples which suggest the desired results of a successful use of the claimed protein and 4) the relative skill of those in the art is commonly recognized as quite high (post - doctoral level).

In view of all of the above, it is determined that the specification has not provided guidance that would enable one of skill in the art to be able to use the claimed invention commensurate with the claims. One of skill in the art would require undue experimentation to determine whether the claimed 67 kDa protein can be used to treat or inhibit anthrax toxins *in vivo.*

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-8 and 21 are rejected under 35 U.S.C. 102(a) as anticipated by Bijl et al *(Clin. Exp. Allergy, January 2003, 33:65-71).*

Claims 1-8 and 21 are directed to a novel protein capable of inhibiting anthrax toxin activity.

Bijl et al teach a 67kDa protein purified from *Imperata cylindrica* (page 65). Bijl et al teach a protein that is stable at room temperature (see Abstract). Bijl et al teach a 67kDa protein binds IgE (page 68). Claims limitations such as "hydrophobic in nature", "resistant to trypsin", "has no proteolytic acitivity", "inhibits proteolytic cleavage of protective antigen (PA) of *B. anthracis* in a dose dependent manner", "is devoid of any carbohydrate moiety", "wherein the range of about 25-20 ng completely inhibits the cleavage of the protective antigen of *B. anthracis* by trypsin" wherein protein in the range of about 15-5 ng completely inhibits the cleavage of the protective antigen of *B. anthracis* by trypsin", "wherein

the protein in the range of about 25 ng to 11, 000 ng is effective in inhibiting the anthrax activity" and "wherein the protein in the range of about 50 to 10, 000 ng is effective in inhibiting anthrax activity" would be inherent in the teachings of the prior art.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

8. Claims 1-8 and 21 are rejected under 35 U.S.C. 102(b) as anticipated by Bijl et al *(Journal of Immunological Methods 260 (Feb. 2002, 91-96).*

Claims 1-8 and 21 are directed to a novel protein capable of inhibiting anthrax toxin activity.

Bijl et al teach a 67kDa protein purified from *Imperata cylindrica* that binds IgE (page 93, Figures 1 (a)-(c)). Bijl et al teach a protein that is stable at room temperature (page 92). Claims limitations such as "hydrophobic in nature", "resistant to trypsin", "has no proteolytic acitivity", "inhibits proteolytic cleavage of protective antigen (PA) of *B. anthracis* in a dose dependent manner" and "is devoid of any carbohydrate moiety", wherein the range of about 25-20 ng completely inhibits the cleavage of the protective antigen of *B. anthracis* by

trypsin" "wherein protein in the range of about 15-5 ng completely inhibits the cleavage of the protective antigen of *B. anthracis* by trypsin", "wherein the protein in the range of about 25 ng to 11, 000 ng is effective in inhibiting the anthrax activity" and "wherein the protein in the range of about 50 to 10, 000 ng is effective in inhibiting anthrax activity" would be inherent in the teachings of the prior art.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

9. Claims 1-8 and 21 are rejected under 35 U.S.C. 102(b) as anticipated by Verma et al *(International Archives of Allergy and Immunology, 200, 122:251-256).*

Claims 1-8 and 21 are directed to a novel protein capable of inhibiting anthrax toxin activity.

Verma et al teach a 67kDa protein purified from *Imperata cylindrica* that binds IgE (page 252). Bijl et al teach a protein that is stable at room temperature (page 252). Claims limitations such as "hydrophobic in nature", "resistant to trypsin", "has no proteolytic acitivity", "inhibits proteolytic cleavage of protective

antigen (PA) of *B. anthracis* in a dose dependent manner" and "is devoid of any carbohydrate moiety", wherein the range of about 25-20 ng completely inhibits the cleavage of the protective antigen of *B. anthracis* by trypsin" wherein protein in the range of about 15-5 ng completely inhibits the cleavage of the protective antigen of *B. anthracis* by trypsin", "wherein the protein in the range of about 25 ng to 11, 000 ng is effective in inhibiting the anthrax activity" and "wherein the protein in the range of about 50 to 10, 000 ng is effective in inhibiting anthrax activity" would be inherent in the teachings of the prior art.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of Claims

10. No claims are allowed.

Conclusion

11. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
November 20, 2004

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PRIMARY EXAMINER